Table 24-1. Factors that affect renin secretion.

Stimulatory
Increased sympathetic activity via renal nerves
Increased circulating catecholamines
Prostaglandins
Inhibitory
Increased Na^+ and Cl^- reabsorption across macula densa
Increased afferent arteriolar pressure
Angiotensin II
Vasopressin

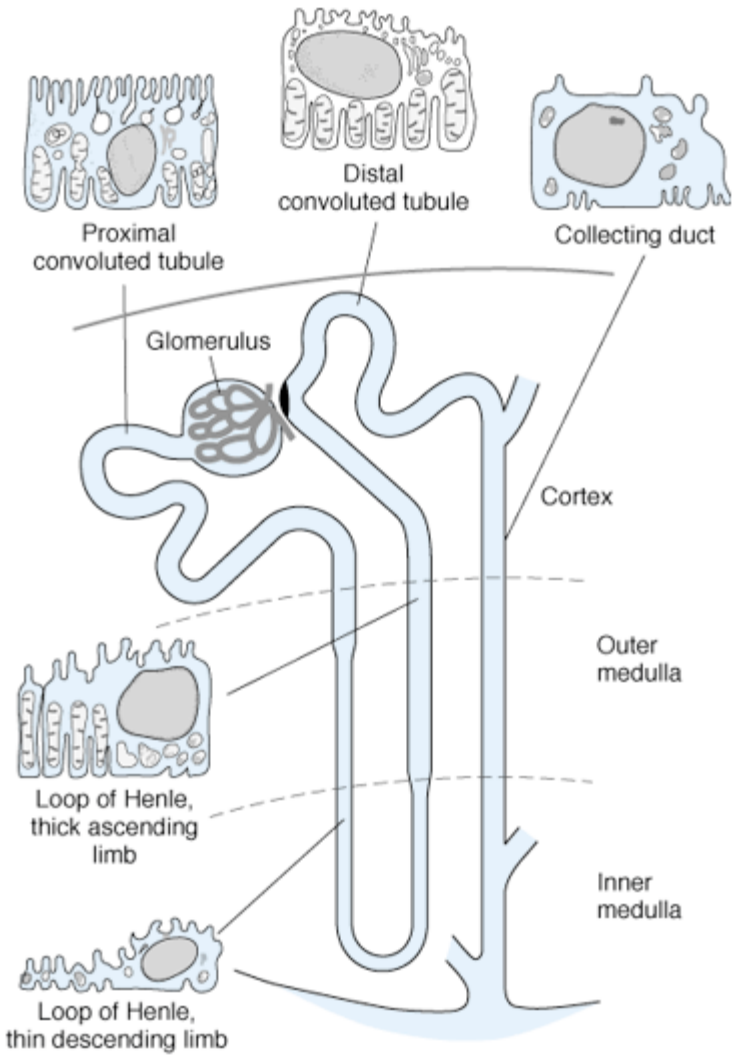
Table 38-3. Agents causing contraction or relaxation of mesangial cells.

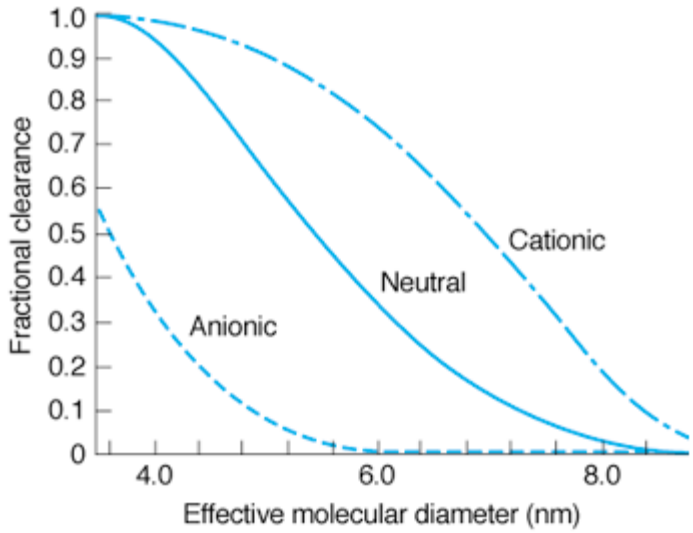
Contraction	Relaxation
Endothelins	
Angiotensin II	ANP
Vasopressin	Dopamine
Norepinephrine	PGE_2
Platelet-activating factor	cAMP
Platelet-derived growth factor	
Thromboxane A_2	
PGF_2	
Leukotrienes C_4 and D_4	
Histamine	

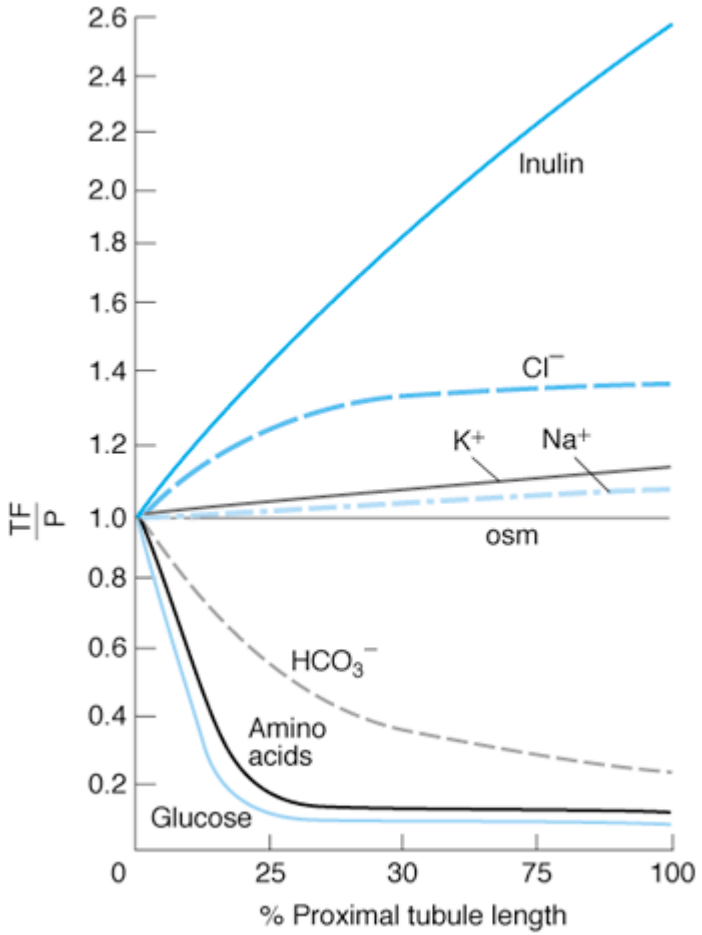
Table 38-5. Renal handling of various plasma constituents in a normal adult human on an average diet.

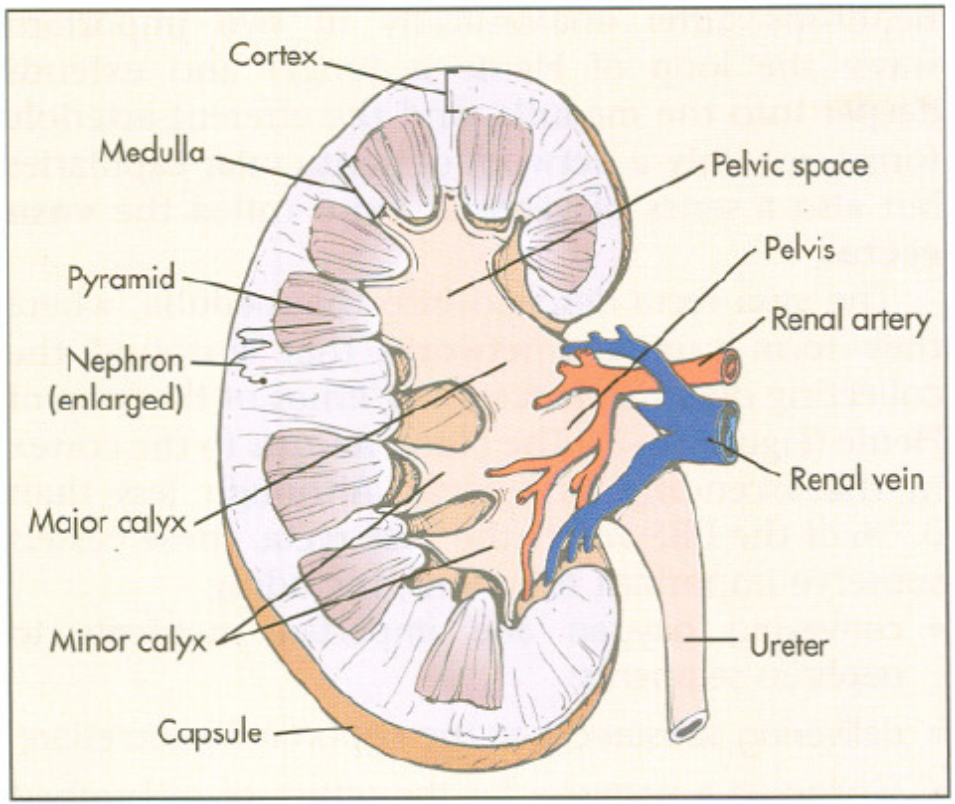
Substance	Per 24 Hours				Percentage Reabsorbed	Location[1]
	Filtered	Reabsorbed	Secreted	Excreted		
Na^+ (meq)	26,000	25,850		150	99.4	P, L, D, C
K^+ (meq)	600	560[2]	50[2]	90	93.3	P, L, D, C
Cl^- (meq)	18,000	17,850		150	99.2	P, L, D, C
HCO_3^- (meq)	4,900	4,900		0	100	P, D
Urea (mmol)	870	460[3]		410	53	P, L, D, C
Creatinine (mmol)	12	1[4]	1[4]	12		
Uric acid (mmol)	50	49	4	5	98	P
Glucose (mmol)	800	800		0	100	P
Total solute (mosm)	54,000	53,400	100	700	98.9	P, L, D, C
Water (mL)	180,000	179,000		1000	99.4	P, L, D, C

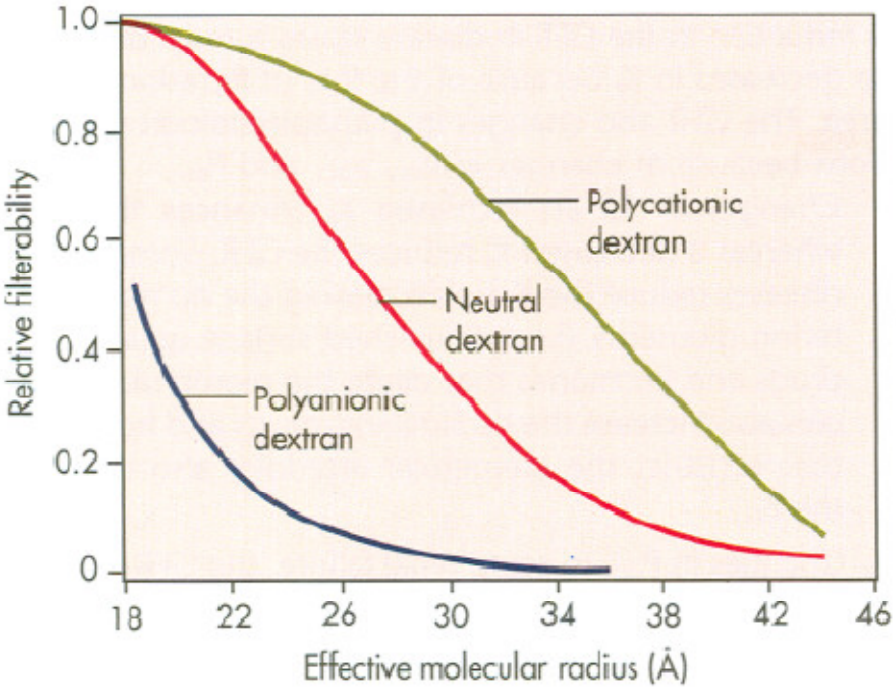
[1] P, proximal tubules; L, loops of Henle; D, distal tubules; C, collecting ducts.

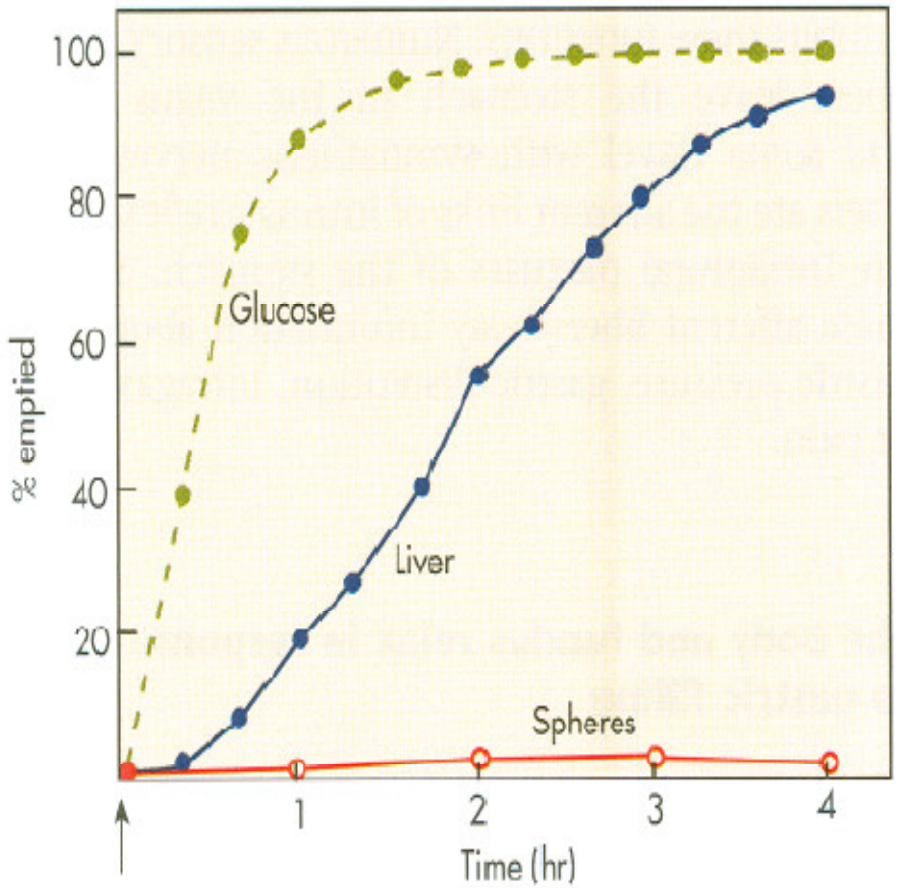

Distal
convoluted tubule
Proximal
convoluted tubule
Collecting duct
Glomerulus
Cortex
Outer
medulla
Loop of Henle,
thick ascending
limb
Inner
medulla
Loop of Henle,
thin descending limb


1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
Fractional clearance
Cationic
Neutral
Anionic
4.0
6.0
8.0
Effective molecular diameter (nm)


2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0
25
30
75
100
TF/P
% Proximal tubule length
Inulin
Cl⁻
K⁺
Na⁺
osm
HCO3⁻
Amino acids
Glucose


Cortex
Medulla
Pyramid
Nephron
(enlarged)
Major calyx
Minor calyx
Capsule
Pelvic space
Pelvis
Renal artery
Renal vein
Ureter


1.0
0.8
0.6
0.4
0.2
0
Relative filterability
Polycationic dextran
Neutral dextran
Polyanionic dextran
18
22
26
30
34
38
42
46
Effective molecular radius (Å)


100
80
60
40
20
% emptied
Glucose
Liver
Spheres
1
2
3
4
Time (hr)

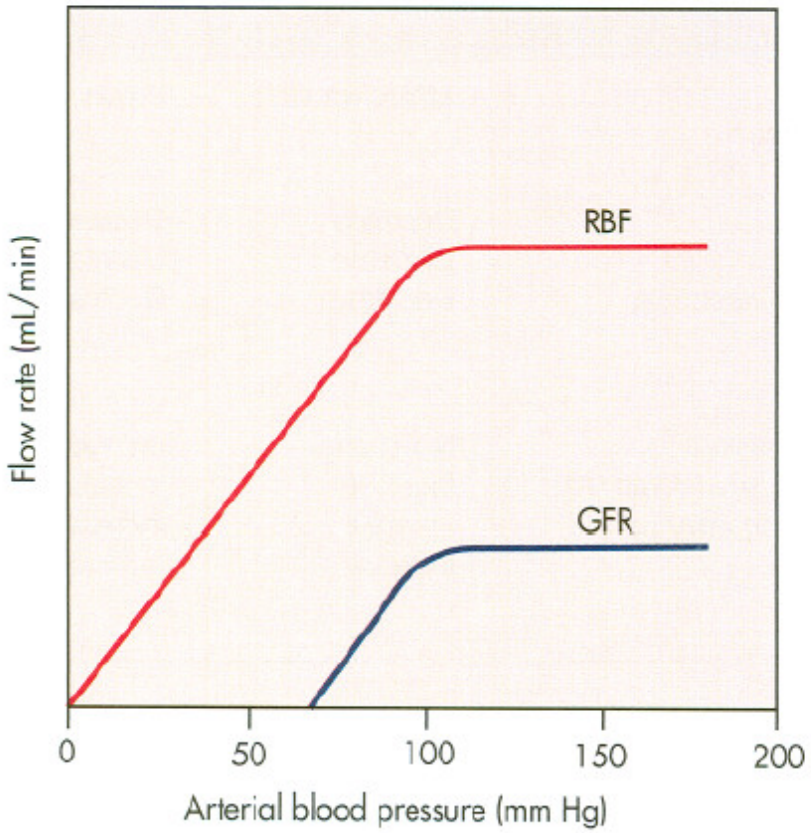
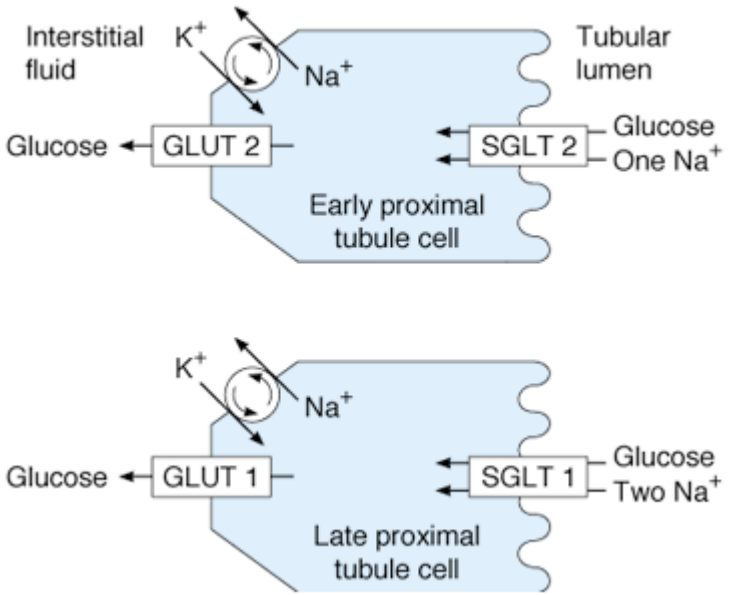


FIGURE 36–12. Relationship between arterial blood pressure and RBF and between arterial blood pressure and GFR. Autoregulation maintains the GFR and RBF


Interstitial fluid
K^+
Na^+
Tubular lumen
Glucose
GLUT 2
SGLT 2
Glucose
One Na^+
Early proximal tubule cell
K^+
Na^+
Glucose
GLUT 1
SGLT 1
Glucose
Two Na^+
Late proximal tubule cell

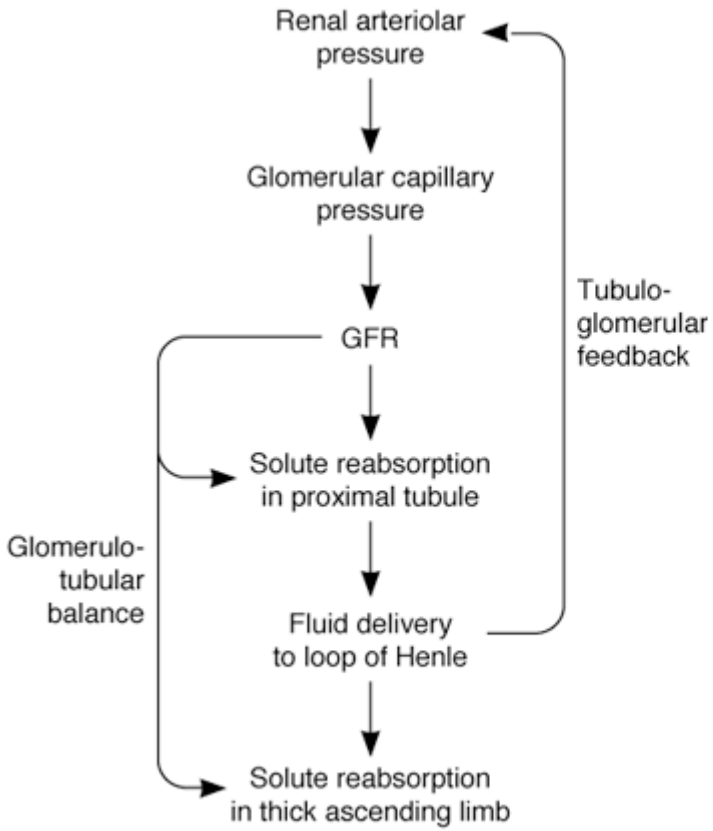


Figure 38-14. Mechanisms of glomerulotubular balance and tubuloglomerular feedback.

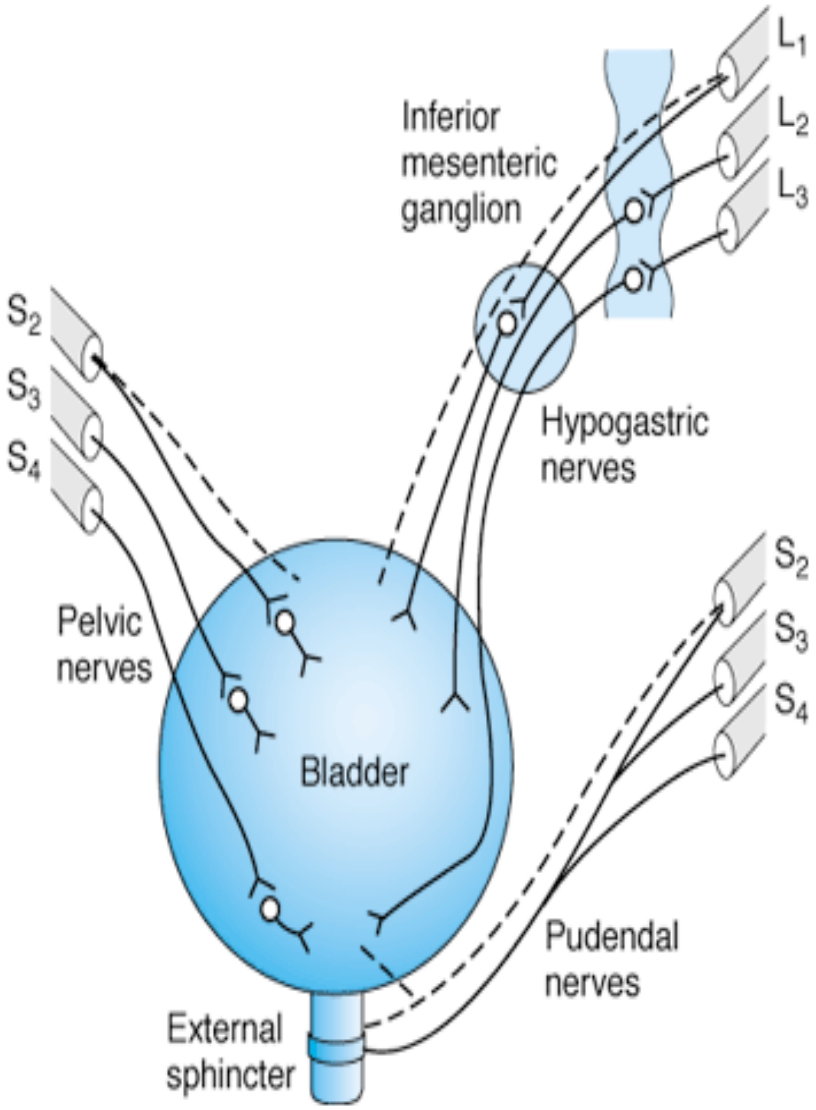


Figure 38-25. Innervation of the bladder. Dashed lines indicate sensory nerves. Parasympathetic innervation is shown at the left, sympathetic at the upper right, and somatic at the lower right.

Table 39-2. Principal buffers in body fluids.

Blood	$H_2CO_3 \leftrightarrows H^+ + HCO_3^-$ $HProt \leftrightarrows H^+ Prot^-$ $HHb \leftrightarrows H^+ Hb^-$
Interstitial fluid	$H_2CO_3 \leftrightarrows H^+ + HCO_3^-$
Intracellular fluid	$HProt \leftrightarrows H^+ Prot^-$ $H_2PO_4^- \leftrightarrows H^+ + HPO_4^{2-}$

Table 39-3. Plasma pH, HCO_3^-, and P_{CO2} values in various typical disturbances of acid-base balance.[1]

Condition	Arterial Plasma			
	pH	HCO_3^- (meq/L)	P_{CO2} (mm Hg)	Cause
NORMAL	7.40	24.1	40	
Metabolic acidosis	7.28	18.1	40	NH_4Cl ingestion
	6.96	5.0	23	Diabetic acidosis
Metabolic alkalosis	7.50	30.1	40	$NaHCO_3$ ingestion
	7.56	49.8	58	Prolonged vomiting
Respiratory acidosis	7.34	25.0	48	Breathing 7% CO_2
	7.34	33.5	64	Emphysema
Respiratory alkalosis	7.53	22.0	27	Voluntary hyperventilation
	7.48	18.7	26	Three-week residence at 4000-m altitude

[1] In the diabetic acidosis and prolonged vomiting examples, respiratory compensation for primary metabolic acidosis and alkalosis has occurred, and the P_{CO2} has shifted from 40 mm Hg. In the emphysema and high-altitude examples, renal compensation for primary respiratory acidosis and alkalosis has occurred and has made the deviations from normal of the plasma HCO_3^- larger than they would otherwise be.

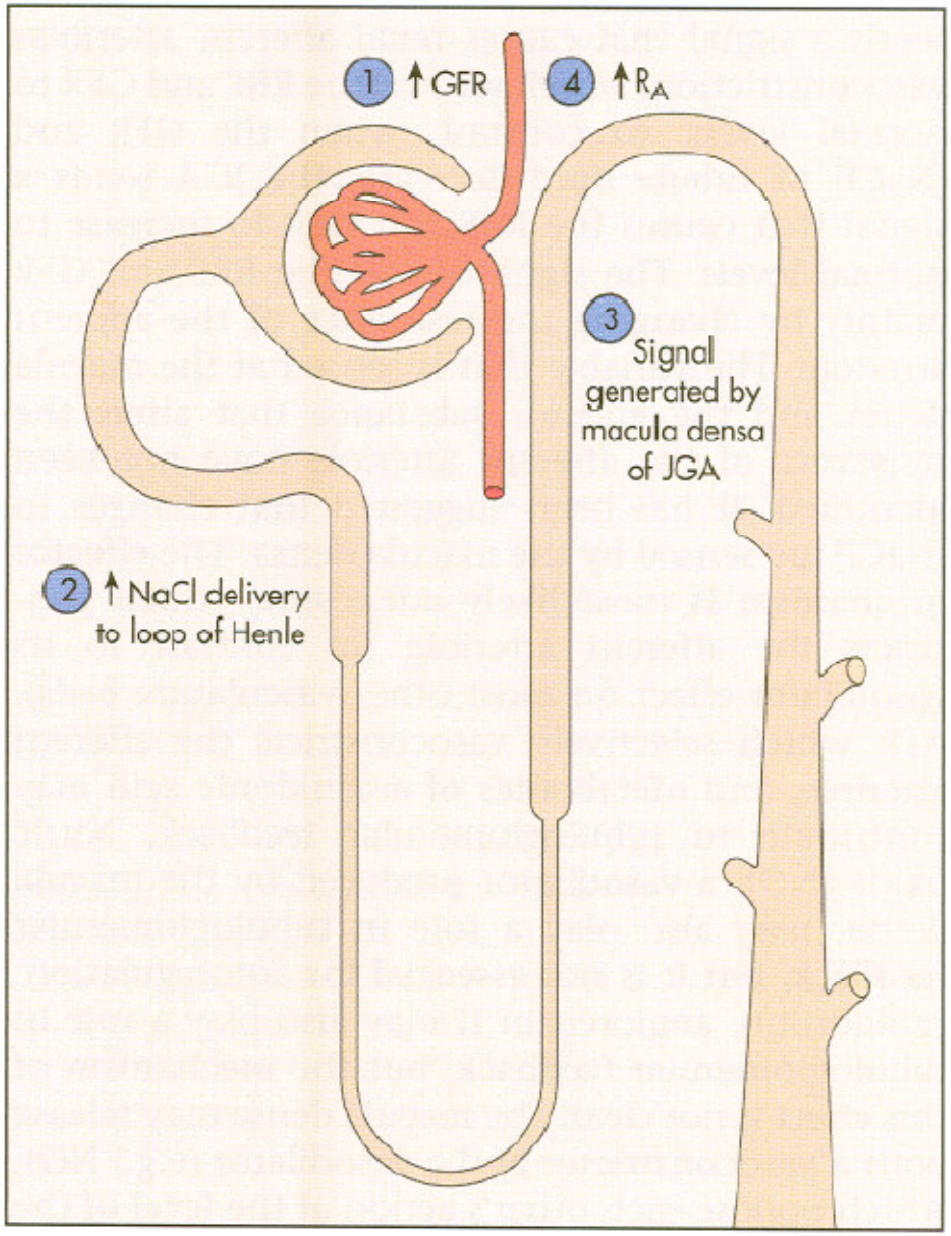


FIGURE 36–13. Tubuloglomerular feedback. An increase

TABLE 36–1. MAJOR HORMONES THAT INFLUENCE GLOMERULAR FILTRATION RATE AND RENAL BLOOD FLOW

	Stimulus	Effect on GFR	Effect on RBF
Vasoconstrictors			
Sympathetic nerves	Decreased ECFV	Decrease	Decrease
Angiotensin II	Decreased ECFV	Decrease	Decrease
Endothelin	Increased stretch, angiotensin II, bradykinin, epinephrine; decreased ECFV	Decrease	Decrease
Vasodilators			
Prostaglandins	Decreased ECFV; increased shear stress, angiotensin II	No change	Increase
Nitric oxide	Increased shear stress, acetylcholine, histamine, bradykinin, ATP	Increase	Increase
Bradykinin	Prostaglandins, decreased angiotensin-converting enzyme	Increase	Increase
Atrial natriuretic peptide, brain natriuretic peptide	Increased ECFV	Increase	Increase

ECFV, extracellular fluid volume.

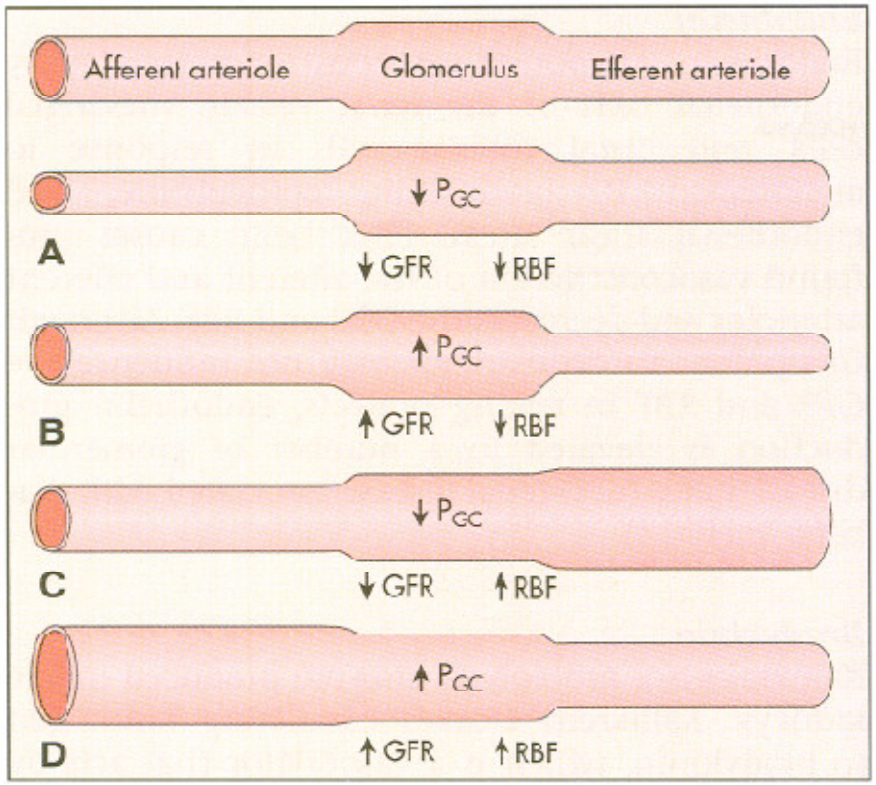


FIGURE 36–14. Relationship between selective changes in the resistance of either the afferent arteriole or the efferent arteriole on RBF and GFR. Constriction of either

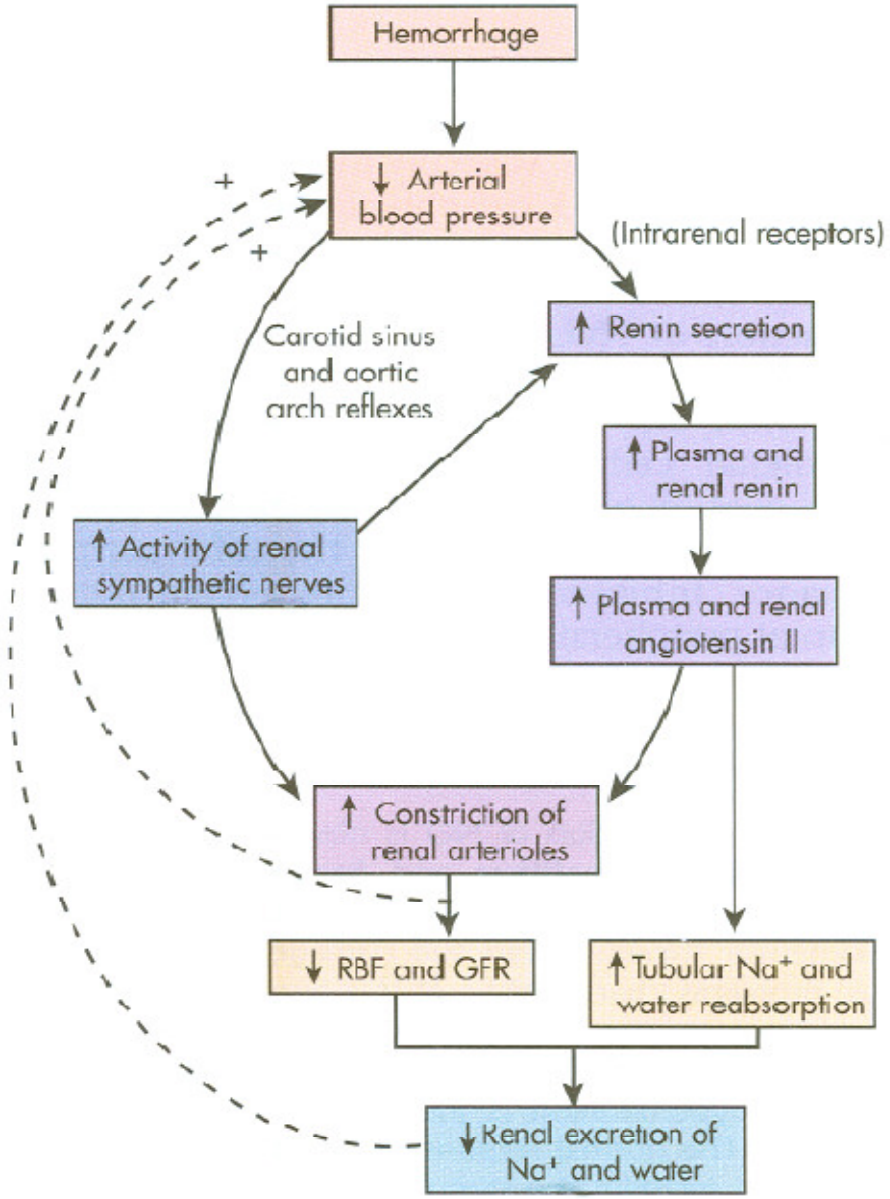


FIGURE 36–15. Pathway by which hemorrhage activates renal sympathetic nerve activity and stimulates the production of angiotensin II. (Modified from Vander AJ:

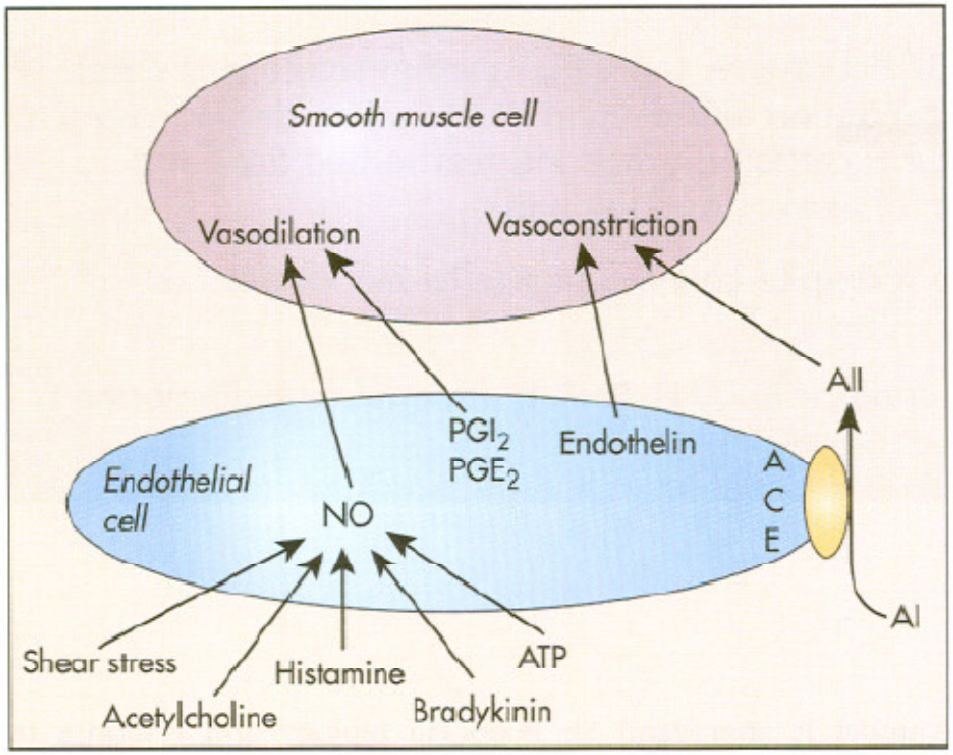


FIGURE 36–16. Examples of the interactions of endothelial cells with smooth muscle or mesangial cells. ACE,

TABLE 37–1. FILTRATION, EXCRETION, AND REABSORPTION OF WATER, ELECTROLYTES, AND SOLUTES BY THE KIDNEYS

Substance	Measure	Filtered*	Excreted	Reabsorbed	Filtered Load Reabsorbed (%)
Water	L/day	180	1.5	178.5	99.2
Na^+	mEq/day	25,200	150	25,050	99.4
K^+	mEq/day	720	100	620	86.1
Ca^{++}	mEq/day	540	10	530	98.2
HCO_3^-	mEq/day	4320	2	4318	99.9+
Cl^-	mEq/day	18,000	150	17,850	99.2
Glucose	mmol/day	800	0	800	100.0
Urea	g/day	56	28	28	50.0

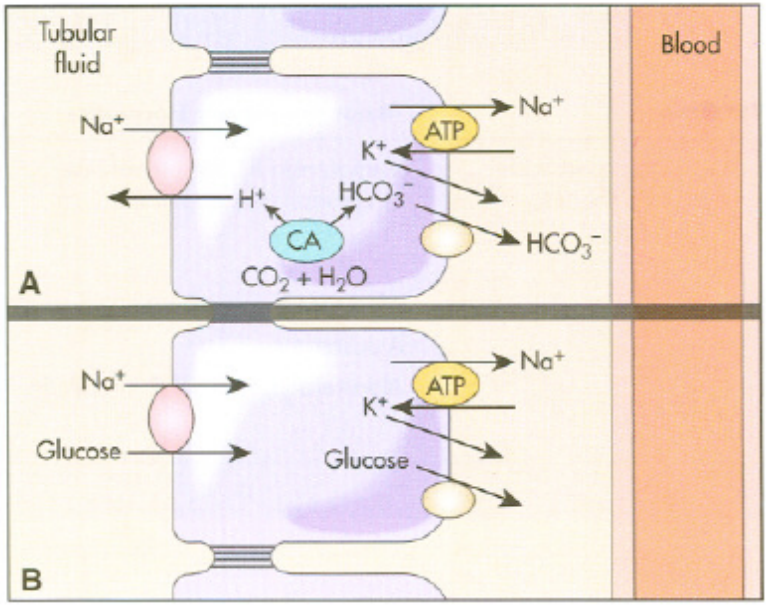
*The filtered amount of any substance is calculated by multiplying the concentration of that substance in the ultrafiltrate by the glomerular filtration rate (GFR); for example, the filtered load of Na^+ is calculated as $[Na^+]_{ultrafiltrate}$ (140 mEq/L) × GFR (180 L/day) = 25,200 mEq/day.

TABLE 37–2. COMPOSITION OF URINE

Substance	Concentration
Na^+	50-130 mEq/L
K^-	20-70 mEq/L
Ammorium	30-50 mEq/L
Ca^{++}	5-12 mEq/L
Mg^{++}	2-18 mEq/L
Cl^-	50-130 mEq/L
Inorganic phosphate	20-40 mEq/L
Urea	200-400 mM
Creatinine	6-20 mM
pH	5.0-7.0
Osmolality	500-800 mOsm/kg H_2O
Glucose	0
Amino acids	0
Protein	0
Blood	0
Ketones	0
Leukocytes	0
Bilirubir	0

The composition and volume of the urine can vary widely in the healthy state. These values represent average ranges. Water excretion ranges between 0.5 and 1.5 L/day.

Data from Valtin HV: *Renal physiology*, ed 2, Boston, 1983, Little, Brown.



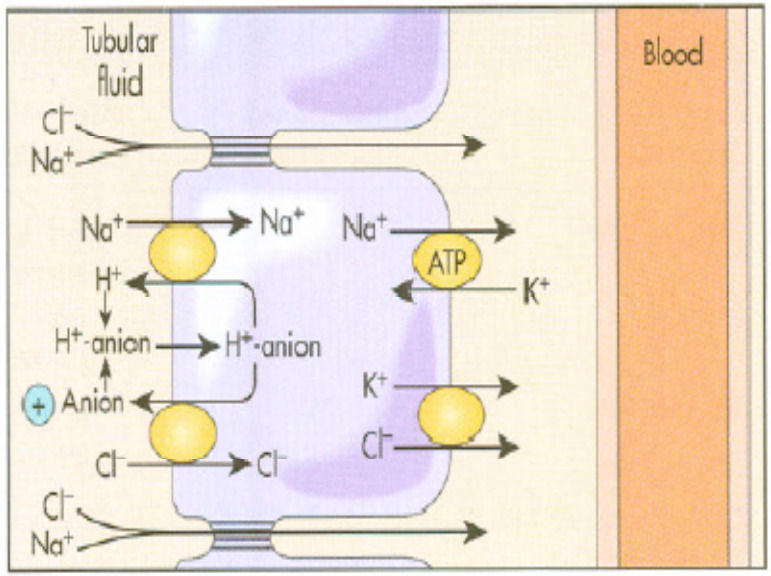


TABLE 37–4. NaCl TRANSPORT ALONG THE NEPHRON

Segment	Filtered Load Reabsorbed (%)	Mechanism of Na^+ Entry Across Apical Membrane	Major Regulatory Hormones
Proximal tubule	67	Na^+-H^+ exchange, Na^+ cotransport with amino acids and organic solutes, Na^+-H^+/Cl^--anion exchange, paracellular	Angiotensin II, norepinephrine, epinephrine, dopamine
Loop of Henle	25	1Na^+,1K^+,2Cl^- symport	Aldosterone
Distal tubule	≈4	NaCl symport	Aldosterone
Late distal tubule and collecting duct	≈3	Na^+ channels	Aldosterone, ANP, BNP, urodilatin

ANP, atrial natriuretic peptide; BNP, brain natriuretic peptide.

TABLE 37–5. WATER TRANSPORT ALONG THE NEPHRON

Segment	Filtered Load Reabsorbed (%)	Mechanism of Water Reabsorption	Hormones That Regulate Water Permeability
Proximal tubule	67	Passive	None
Loop of Henle	15	Descending thin limb only; passive	None
Distal tubule	0	No water reabsorption	None
Late distal tubule and collecting duct	≈8-17	Passive	ADH, ANP, BNP*

*Atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP) inhibit ADH-stimulated water permeability.

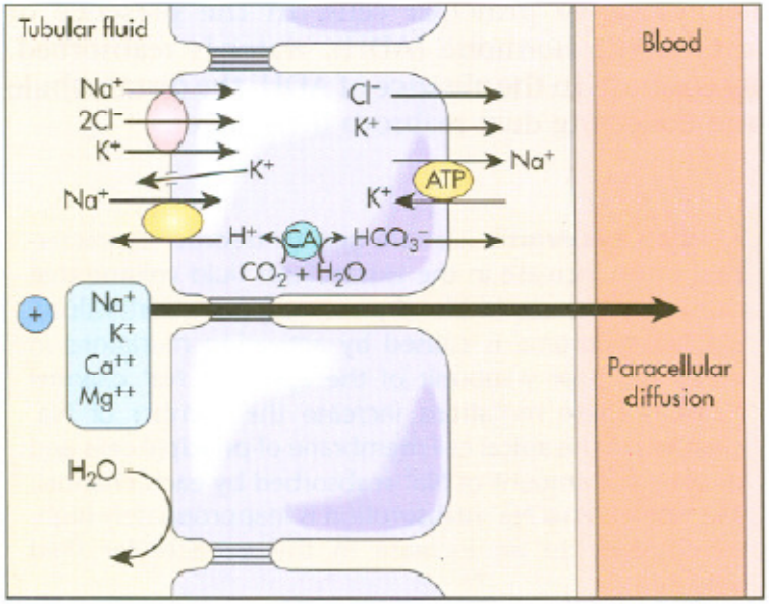


FIGURE 37–4. Transport mechanisms for NaCl reabsorption in the thick ascending limb of the loop of Henle. The positive charge in the lumen plays a major role in driving the passive paracellular reabsorption of cations. Muta-

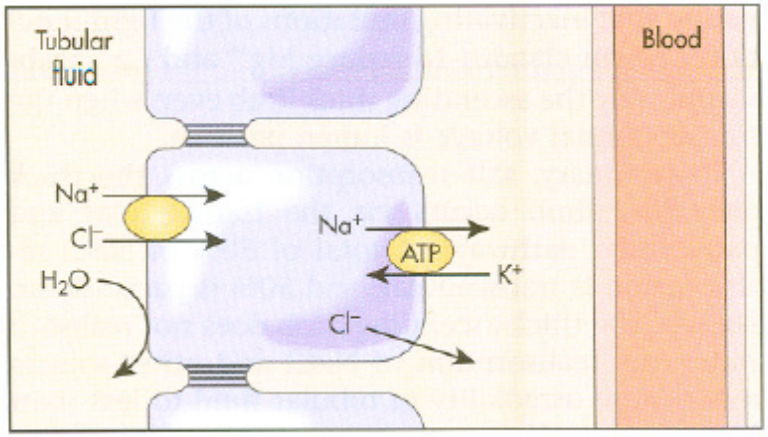


FIGURE 37–5. Transport mechanism for Na^+ and Cl^- reabsorption in the early segment of the distal tubule. This segment is impermeable to water.

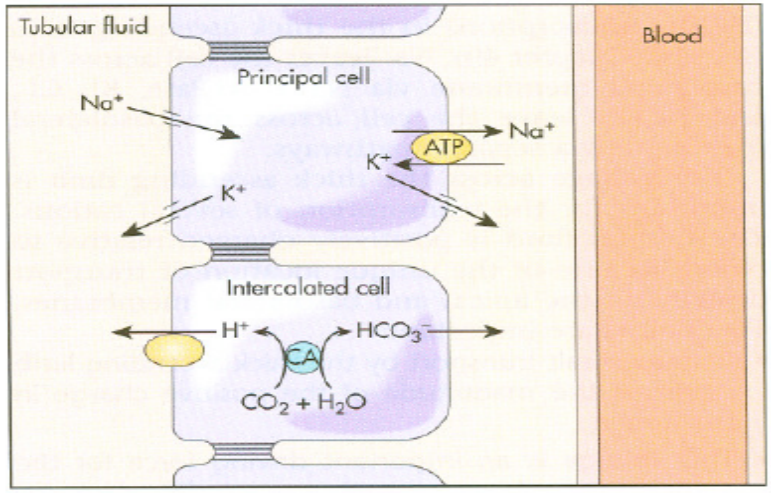


FIGURE 37–6. Transport pathways in principal cells and intercalated cells of the distal tubule and collecting duct. CA, carbonic anhydrase.

TABLE 37–6. HORMONES THAT REGULATE NaCl AND WATER REABSORPTION

Hormone*	Major Stimulus	Nephron Site of Action	Effect on Transport
Angiotensin II	↑Renin	PT	↑NaCl and H_2O reabsorption
Aldosterone	↑Angiotensin II, ↑$[K^+]_p$	TAL, DT/CD	↑NaCl and H_2O reabsorption†
ANP, BNP	↑ECFV	CD	↓H_2O and NaCl reabsorption
Urodilatin	↑ECFV	CD	↓H_2O and NaCl reabsorption
Sympathetic nerves	↓ECFV	PT, TAL, DT/CD	↑NaCl and H_2O reabsorption†
Dopamine	↑ECFV	PT	↓H_2O and NaCl reabsorption
ADH	↑P_{osm}, ↓ECFV	DT/CD	↑H_2O reabsorption†

*All of these hormones act within minutes, except aldosterone, which exerts its action on NaCl reabsorption with a delay of 1 hour.
†The effect on H_2O reabsorption does not include the thick ascending limb.
ANP, atrial natriuretic peptide; BNP, brain natriuretic peptide; CD, collecting duct; DT, distal tubule; ECFV, extracellular fluid volume; $[K^+]_p$, plasma K^+ concentration; P_{osm}, plasma osmolality; PT, proximal tubule; TAL, thick ascending limb; ↑, increase; ↓, decrease.

Control of Body Fluid Osmolality and Extracellular Fluid Volume

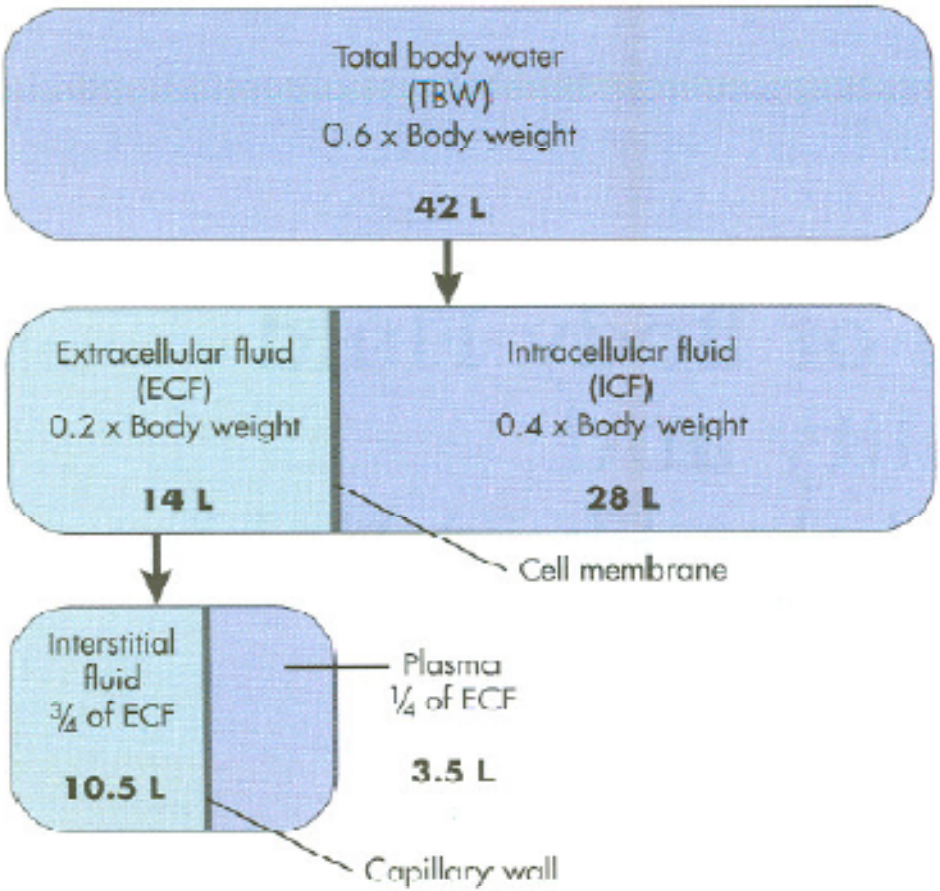


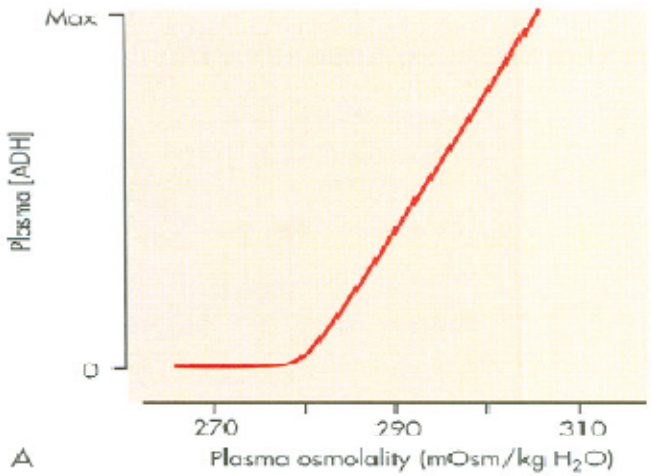
FIGURE 38–1. Relationship among the volumes of the major body fluid compartments. The values shown are calculated for a 70-kg individual.

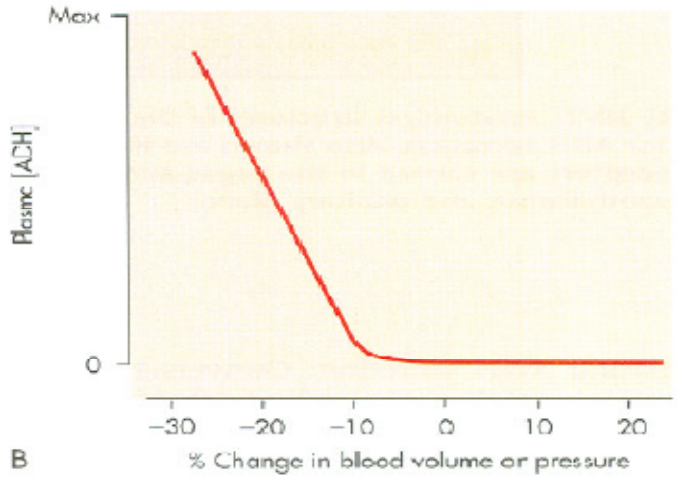
TABLE 38–1. DISTRIBUTION OF SOME CATIONS AND ANIONS IN EXTRACELLULAR AND INTRACELLULAR FLUID

	ECF	ICF*
Na^+ (mEq/L)	145	12
K^+ (mEq/L)	4	150
Ca^{++} (mEq/L)	5	0.001
Cl^- (mEq/L)	105	5
HCO_3^- (mEq/L)	25	12
Inorganic phosphate (Pi)† (mEq/L)	2	100†
pH	7.4	7.1

*The ICF concentrations are estimates from skeletal muscle and include amounts bound to intracellular proteins and free within the cytosol.

†Intracellular phosphate is primarily in the form of organic molecules (e.g., ATP).


Max
Plasma [ADH]
0
270
290
310
A
Plasma osmolality (mOsm/kg H_2O)


Max
Plasma [ADH]
0
−30
−20
−10
0
10
20
B
% Change in blood volume or pressure

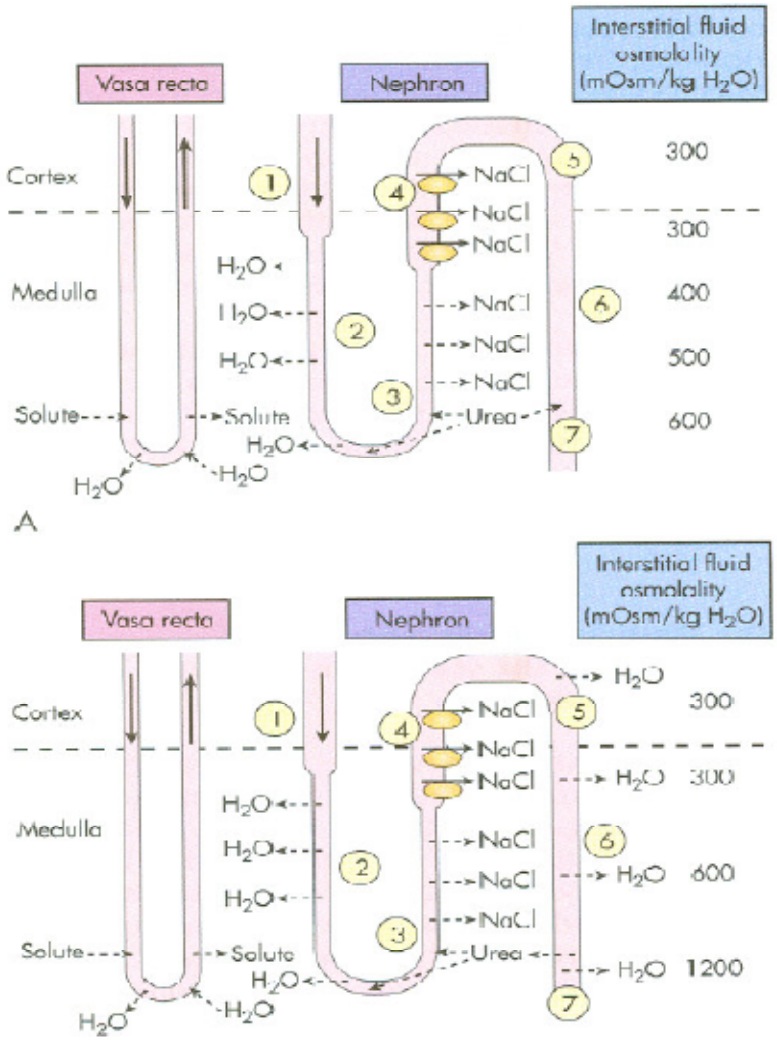


FIGURE 38–4. A, Mechanism for the excretion of dilute urine (water diuresis). ADH is absent, and the collecting duct is essentially impermeable to water. Note that the

TABLE 39–1. NET EFFECTS OF HORMONES AND OTHER FACTORS ON K^+ SECRETION BY THE DISTAL TUBULE AND COLLECTING DUCT

Condition	Direct or Indirect	Flow	Urinary Excretion
Hyperkalemia	Increase	Increase	Increase
Aldosterone			
Acute	Increase	Decrease	No change
Chronic	Increase	No change	Increase
Glucocorticoids	No change	Increase	Increase
ADH	Increase	Decrease	No change
Acidosis			
Acute	Decrease	No change	Decrease
Chronic	Decrease	Large increase	Increase
Alkalosis	Increase	Increase	Large increase

Data from Field MJ, Berliner RW, Giebisch GH. In Narins R, ed: *Textbook of nephrology: clinical disorders of fluid and electrolyte metabolism*, ed 5, New York, 1994, McGraw-Hill.

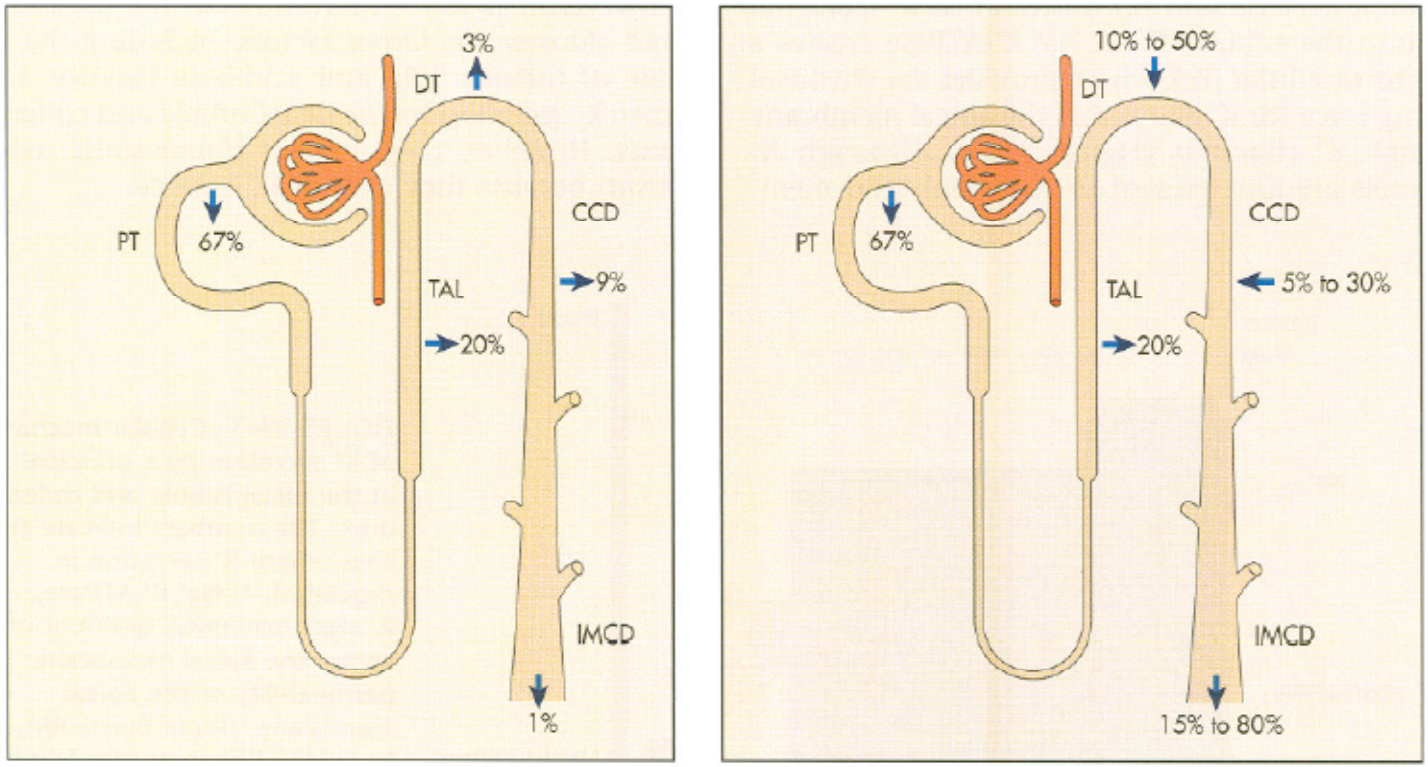


FIGURE 39–2. K^+ transport along the nephron. K^+ excretion depends on the rate and direction of K^+ transport by the distal tubule and collecting duct. Percentages refer to the amount of filtered K^+ reabsorbed or secreted by each nephron

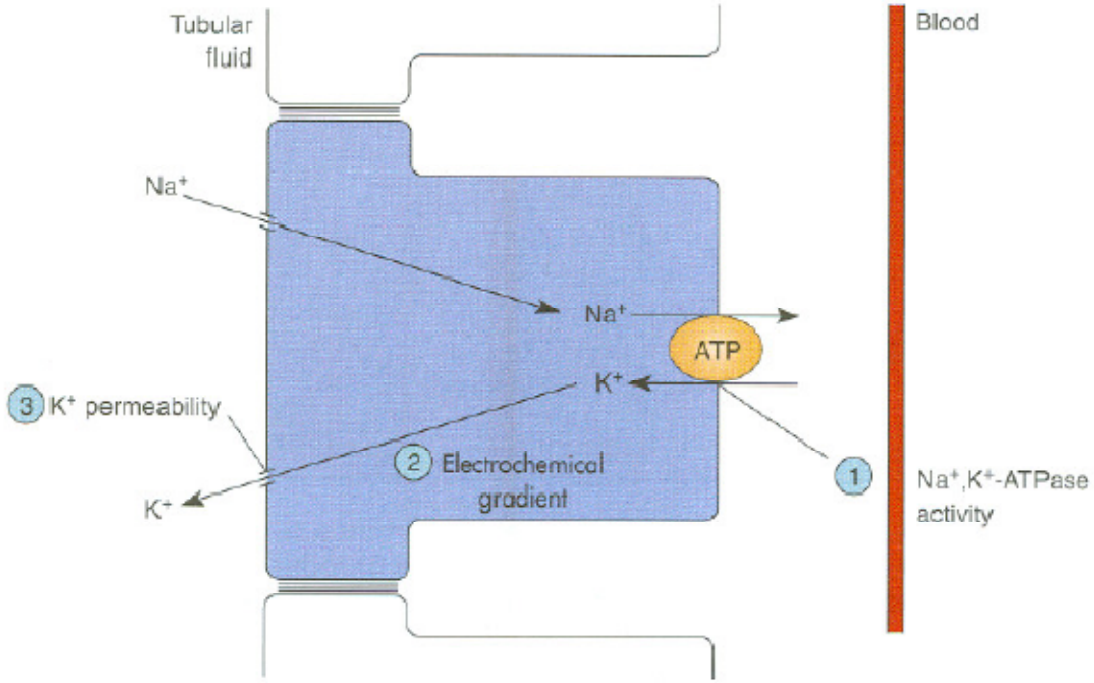


FIGURE 39–3. Cellular mechanism of K^+ secretion by a principal cell in the distal tubule and collecting duct. The numbers indicate the sites where K^+ secretion is regulated. 1, Na^+,K^+-ATPase; 2, electrochemical gradient of K^+ across the apical membrane; 3, K^+ permeability of the apical membrane. (From Berne RM, Levy MN, Koeppen BM, Stanton BA: *Physiology,* ed 5, Philadelphia, 2004, Elsevier.)

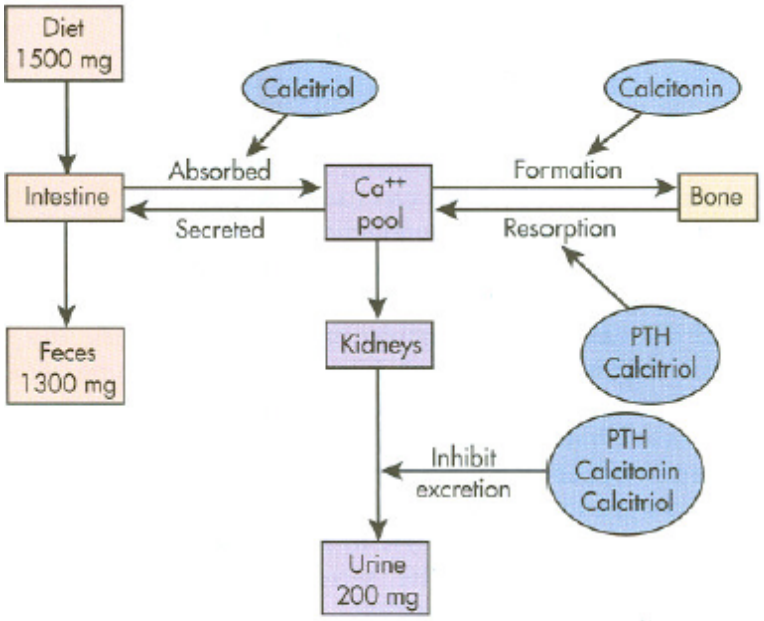


FIGURE 39–4. Overview of Ca^{++} homeostasis. PTH, parathyroid hormone. See text for details.

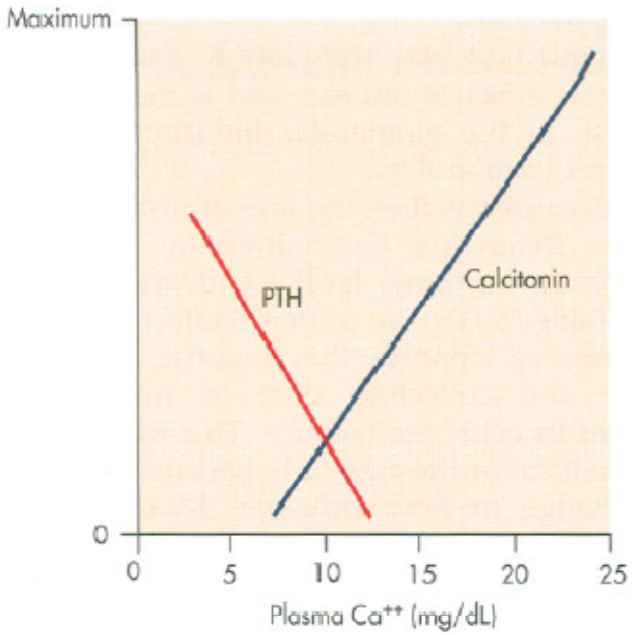


FIGURE 39–5. Effect of the plasma $[Ca^{++}]$ on plasma levels of PTH and calcitonin. (Data from Azria M: *The calcitonins:*

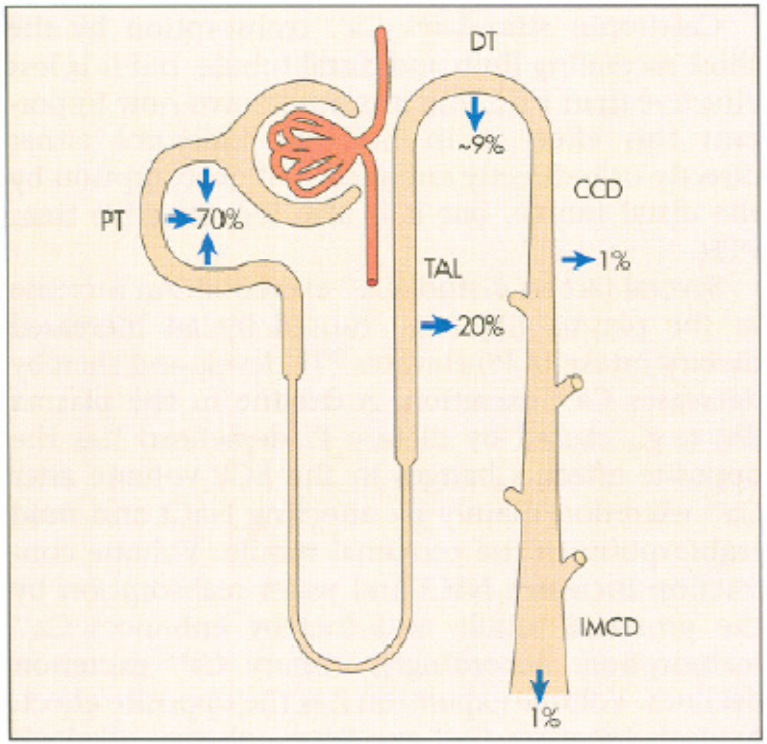


FIGURE 39–6. Ca^{++} transport along the nephron. Per-

TABLE 39–2. SUMMARY OF HORMONES AND FACTORS AFFECTING CA^{++} REABSORPTION

Factor or Hormone	Nephron Location		
	PROXIMAL TUBULE	THICK ASCENDING LIMB	DISTAL TUBULE
Volume expansion	Decrease	No change	Decrease
Hypercalcemia	Decrease	Decrease (CaSR)	Decrease (PTH)
Hypocalcemia	Increase	Increase	
Phosphate loading			Increase (PTH)
Phosphate depletion	Decrease		Decrease (PTH)
Acidosis	Decrease		Decrease
Alkalosis	Increase		
PTH	Increase	Increase	Increase
Vitamin D			Increase
Calcitonin		Increase	Increase

CaSR, calcium-sensing receptor.

Data from Yu AS: Renal transport of calcium, magnesium, and phosphate. In Brenner BM, ed: *Brenner and Rector's the kidney*, ed 7, Philadelphia, 2004, WB Saunders.

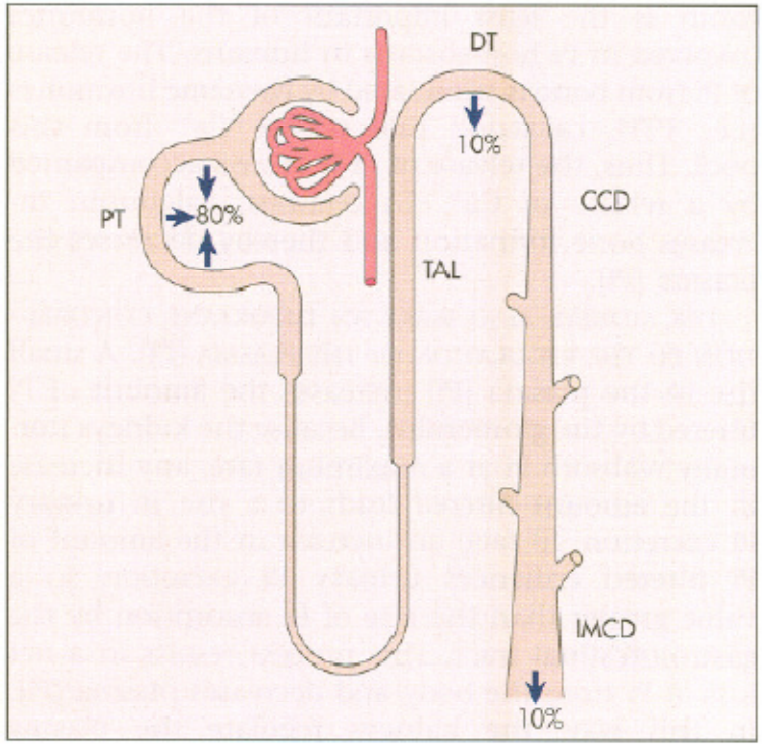


FIGURE 39–8. Pi transport along the nephron. Pi is reabsorbed primarily by the proximal tubule. Percentages

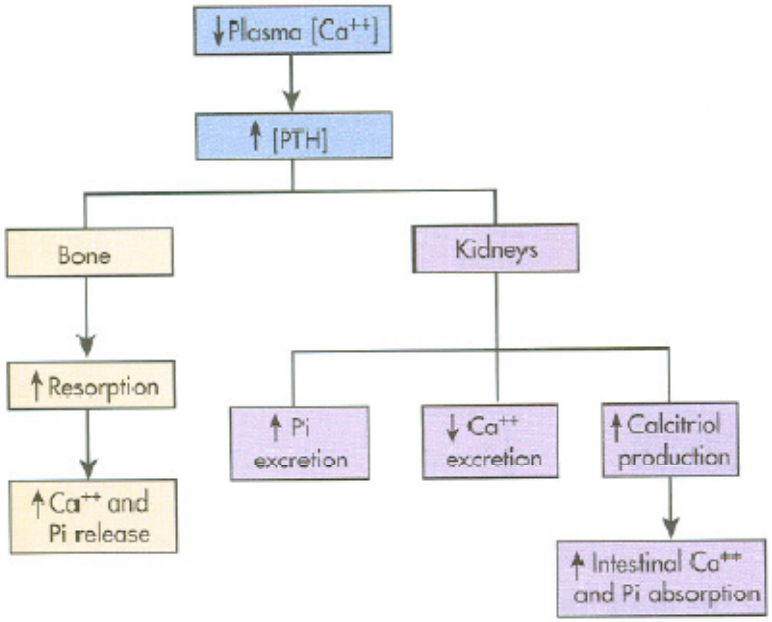


FIGURE 39–9. Effect of PTH on Ca^{++} and Pi homeostasis. The major stimulus of PTH secretion is hypocalcemia.

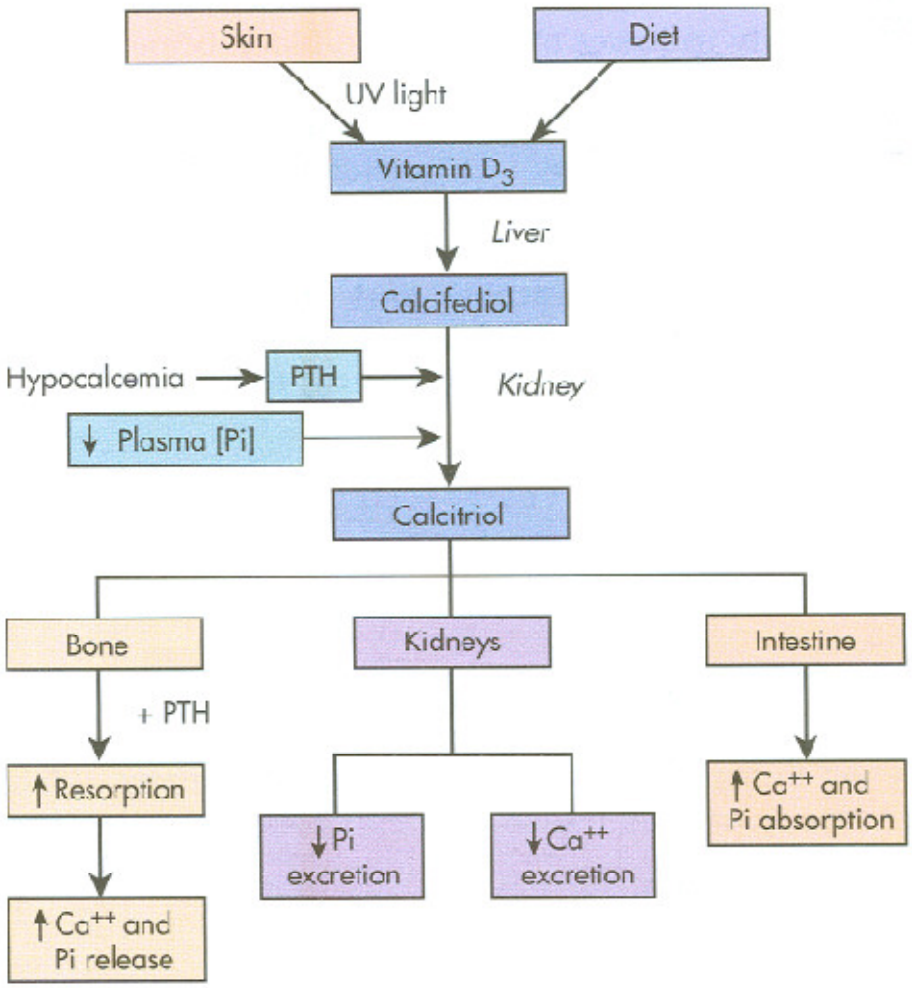
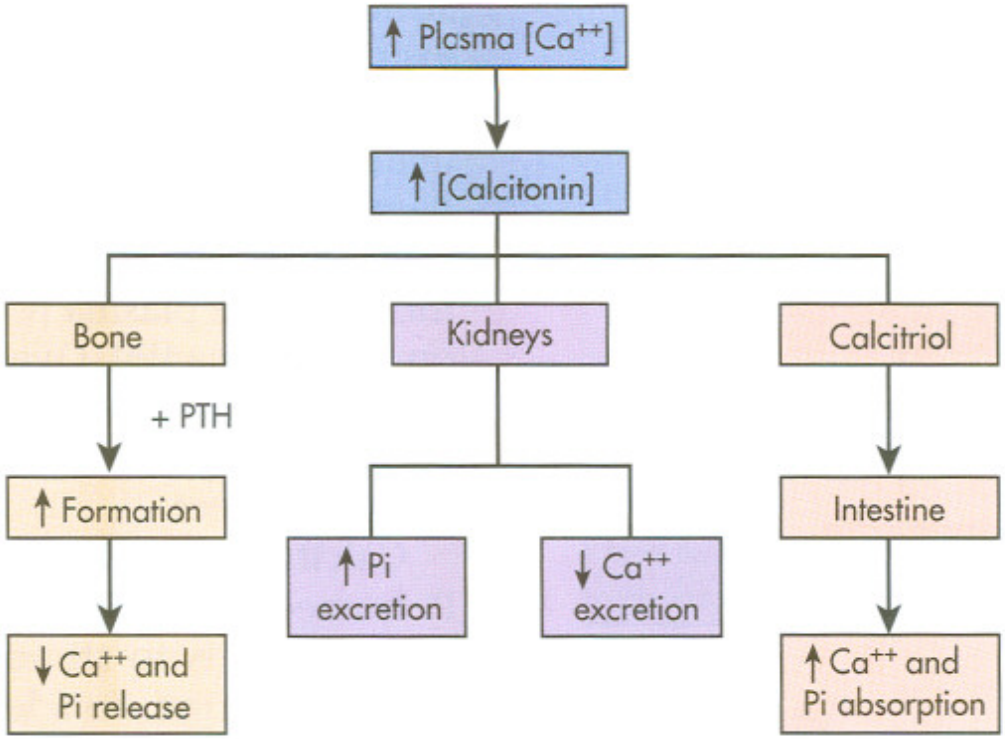


FIGURE 39–10. Activation of vitamin D_3 and its effect on Ca^{++} and Pi metabolism. Hypocalcemia, via PTH, and


↑ Plasma [Ca++]
↑ [Calcitonin]
Bone
Kidneys
Calcitriol
+ PTH
↑ Formation
↑ Pi excretion
↓ Ca++ excretion
Intestine
↓ Ca++ and Pi release
↑ Ca++ and Pi absorption

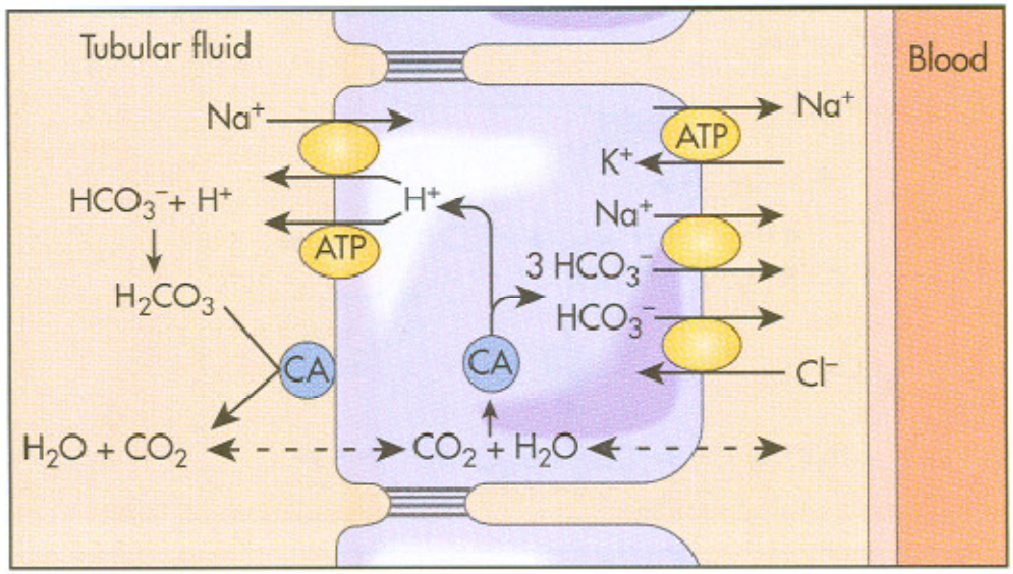


FIGURE 40–1. Cellular mechanism for the reabsorption of filtered HCO_3^- by the cells of the proximal tubule. CA, carbonic anhydrase. See text for details.

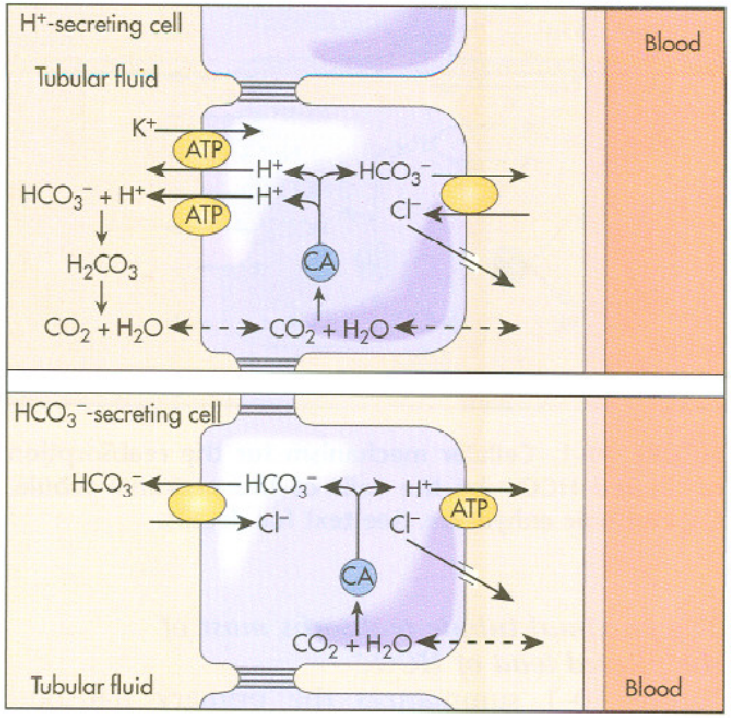


FIGURE 40–2. Cellular mechanisms for the reabsorption and secretion of HCO_3^- by the intercalated cells of the collecting duct. CA, carbonic anhydrase. See text for details.

TABLE 40–1. FACTORS INFLUENCING H^+ SECRETION BY THE NEPHRON

Factor	Principal Site of Action
Increased H^+ Secretion	
Primary	
Decrease in plasma $[HCO_3^-]$ ($\downarrow$pH)	Entire nephron
Increase in P_{CO_2}	Entire nephron
Secondary (not directed at maintaining acid-base balance)	
Increase in filtered load of HCO_3^-	Proximal tubule
Decrease in ECF volume	Proximal tubule
Increase in angiotensin II	Proximal tubule
Increase in aldosterone	Collecting duct
Hypokalemia	Proximal tubule, collecting duct
Decreased H^+ Secretion	
Primary	
Increase in plasma $[HCO_3^-]$ ($\uparrow$pH)	Entire nephron
Decrease in P_{CO_2}	Entire nephron
Secondary (not directed at maintaining acid-base balance)	
Decrease in filtered load of HCO_3^-	Proximal tubule
Increase in ECF volume	Proximal tubule
Decrease in aldosterone	Collecting duct
Hyperkalemia	Proximal tubule
Increase in parathyroid hormone	Proximal tubule

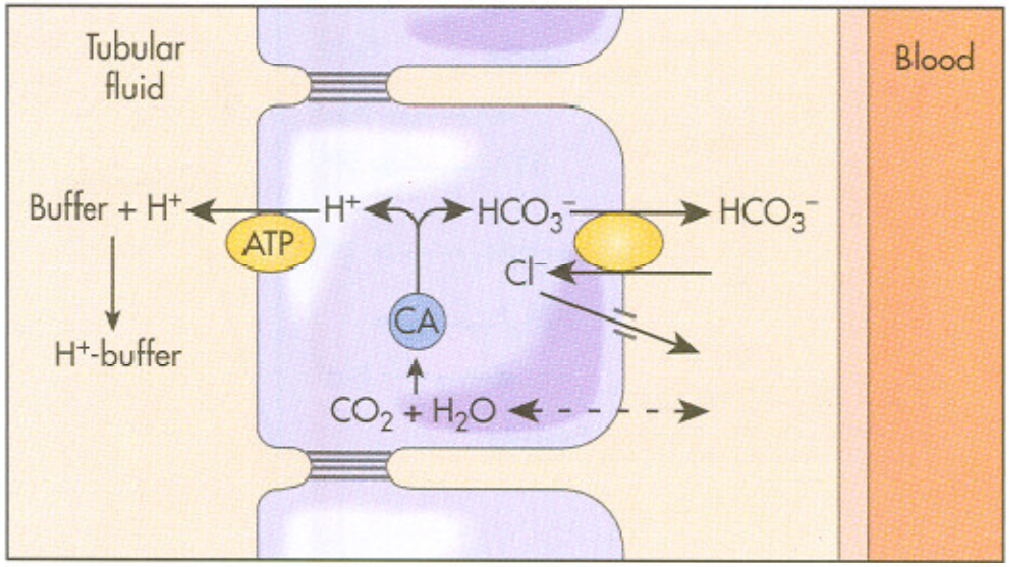


FIGURE 40–3. Excretion of H^+ with non-HCO_3^- urine buffers. The primary urine buffer is phosphate ($HPO_4^=$). Another buffer is creatinine. Collectively, the urine

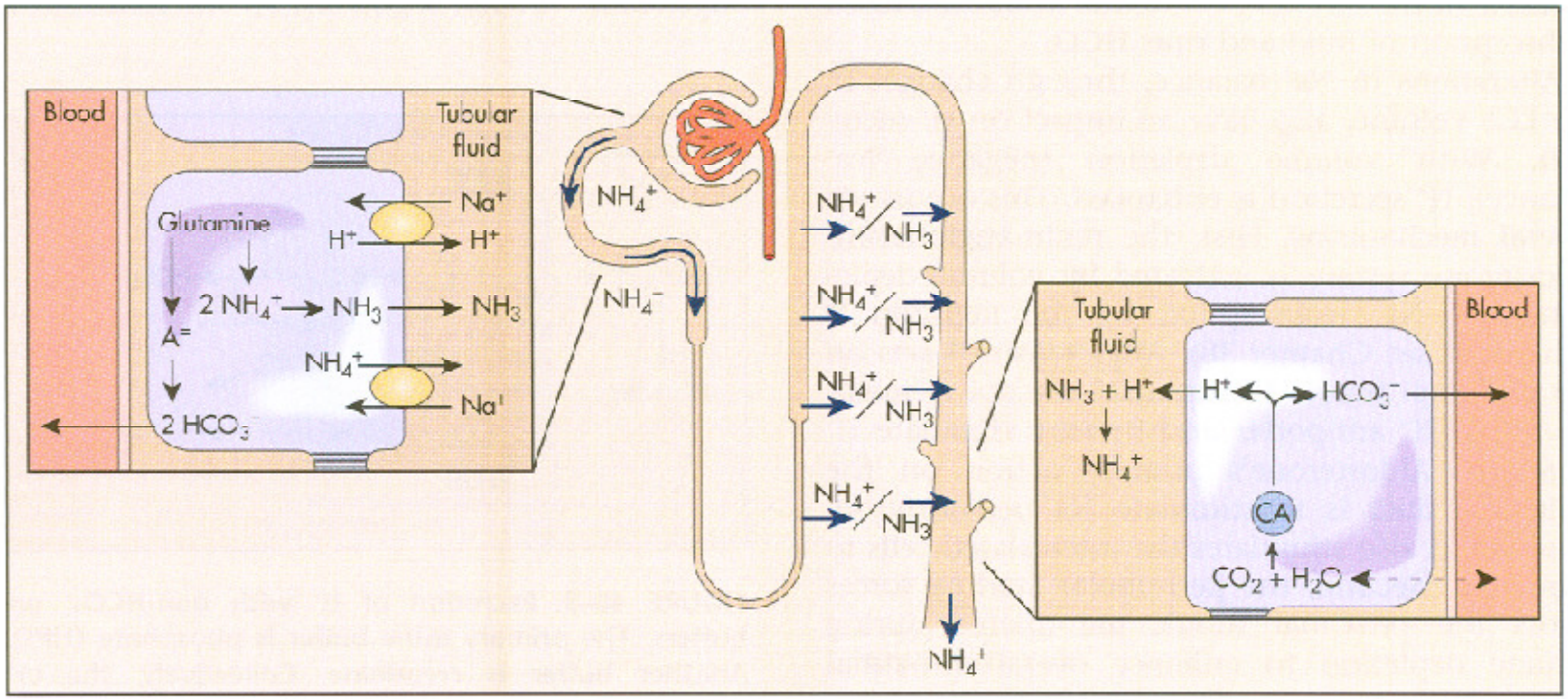
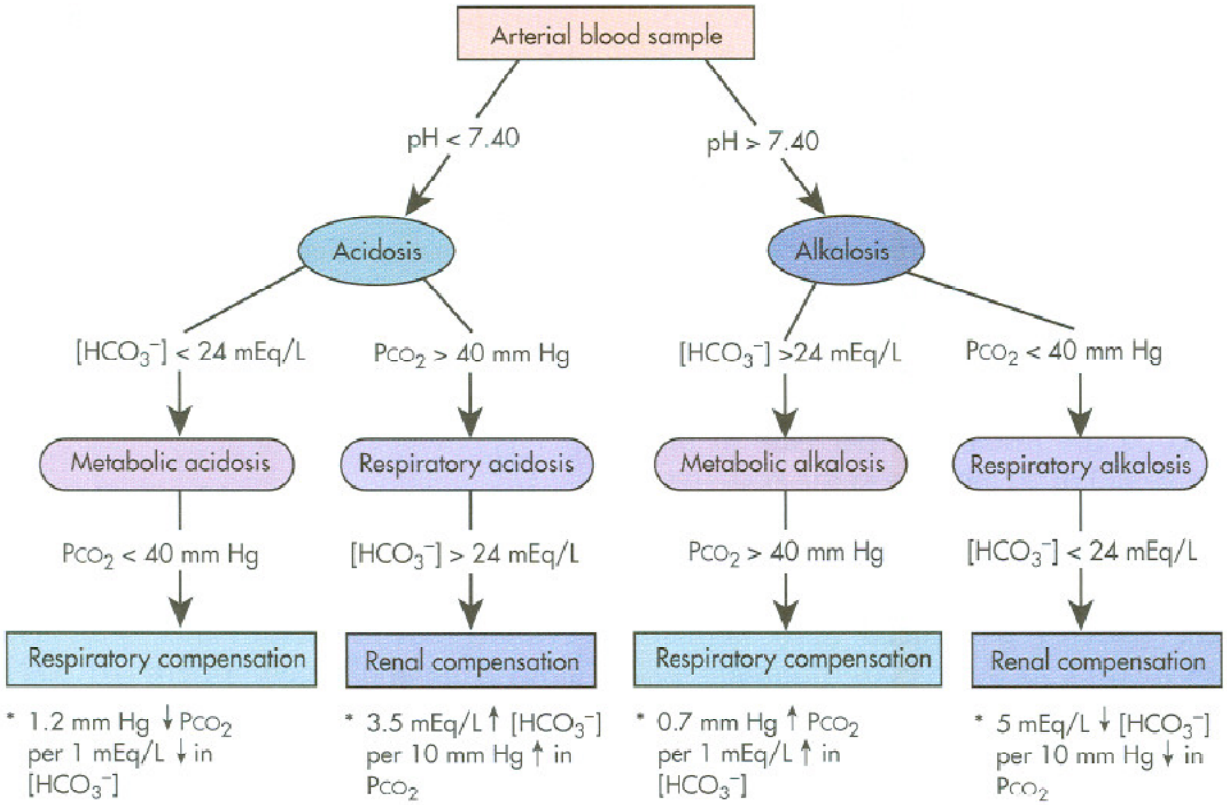


FIGURE 40–4. Production, transport, and excretion of NH_4^+ by the nephron. For every NH_4^+ excreted in the urine, one HCO_3^- is returned to the systemic circulation. See text for details.

TABLE 40–2. MECHANISMS OF DEFENSE AGAINST ACID-BASE DISORDERS

Disorder	Plasma pH	Primary Alteration	Defense Mechanisms
Metabolic acidosis	↓	↓Plasma [HCO_3^-]	ICF and ECF buffers Hyperventilation (↓PCO_2) ↑Renal NAE
Metabolic alkalosis	↑	↑Plasma [HCO_3^-]	ICF and ECF buffers Hypoventilation (↑PCO_2) ↓Renal NAE
Respiratory acidosis	↓	↑PCO_2	ICF buffers ↑Renal NAE
Respiratory alkalosis	↑	↓PCO_2	ICF buffers ↓Renal NAE

NAE, net acid excretion.



RE 40–5. Approach for the analysis of simple acid-base disorders. (*If the compensatory response is not a, a mixed acid-base disorder should be suspected.)